

## **REMARKS**

### **Status of the Claims**

Claims 29 and 31 are amended to be in independent form. Claim 32 is amended to be dependent on claim 29. Claim 24 has been cancelled without prejudice or disclaimer.

No new matter has been added.

Now pending are claims 16-21, 29-32, 36, 40-43, 46-48, 54, 63-65 and 69; claims 16-21 and 29-32 are under examination, and claims 36, 40-43, 46-48, 54, 63-65 and 69 stand withdrawn from consideration.

The amendment and/or cancellation of claims is without prejudice or disclaimer of the subject matter thereof and was done solely to expedite prosecution of the present application. Applicants reserve the right to pursue the original subject matter of this application in a later-filed application claiming benefit of the instant application, including without prejudice to any determination of equivalents of the claimed subject matter.

### **Rejection under 35 U.S.C. §103(a)**

In the Office Action, claims 16-21, 24, and 29-32 were rejected as allegedly unpatentable over John et al., U.S. Patent No. 5,919,934 ("John"), in view of Largent, Mol. Pharmacol. 32:772-784 (1987) ("Largent"). This rejection is traversed.

According to the Office Action, "John teaches sigma receptor imaging agents with a metal chelating group linked to a sigma receptor ligand (i.e., piperidines linked to metal chelators . . . )." While the Office Action concedes that "John does not disclose the dopamine ligand is a 4-phenylpiperidine," the Office Action further states that "Largent discloses that the affinity of sigma receptors for ligands is primarily associated with the 4-phenylpiperidine moiety" and that "the 4-phenylpiperidine can be connected to an n-propyl chain and binds tighter when substituted at this position." The Office Action then concludes that "it would have been prima facie obvious . . . to combine the metal chelating

agent disclosed by John) with the sigma ligands disclosed by Largent in order to obtain a sigma receptor imaging agent.” The Office Action concludes that “the replacement of one art recognized sigma ligand such as the piperidine disclosed by John) with another art recognized sigma receptor ligand (such as the 4-phenylpiperidine of Largent) is merely a substitution of one art known element for another known in the field.” Applicants cannot agree.

The compounds and complexes of the pending claims differ from the compounds of John and Largent. Although the Office Action implies that “replacement of the piperidine disclosed by John” with “the 4-phenylpiperidine of Largent” would result in the compounds of the present claims, Applicants point out that this combination would not result in the compounds or complexes according to the pending claims. For example, the specific compounds disclosed by John include linkers having a carbonyl group attached to the N2S2 chelator moiety (see, e.g., compound K9 of John, cited in the Office Action at page 4), or an amine nitrogen in the linker moiety (a feature also found in cited compound K9), or both a carbonyl group attached to the N2S2 chelator moiety and an amine nitrogen in the linker moiety. The present compounds and complexes do not include such compounds. Thus, one of ordinary skill in the art could not be motivated to modify these specific compounds of John by “replacement of the piperidine disclosed by John” with “the 4-phenylpiperidine of Largent” to arrive at the presently-claimed compounds and complexes; such a combination would not result in the presently-claimed compounds and complexes. Applicants further contend that one of ordinary skill in the art would not be motivated to modify the more general structures disclosed by John as proposed by the Office Action.

Still further, contrary to the assertion in the Office Action, one of ordinary skill in the art would not have had a reasonable expectation of success in making the proposed combination. The John reference provides no guidance regarding the potential activity of substituted piperidine moieties attached to a chelating moiety, because John does not disclose any such compounds.

As to claims 20, 21, and 31, Applicants additionally point out that the claimed compounds and complexes are not 4-phenylpiperidine compounds/complexes. The Office Action has not provided any reasoning to support a conclusion that the compounds of claims 20 and 21, or the complexes of claim 31, would have been obvious in view of the teachings of John or Largent. Applicants respectfully contend that neither John nor Largent teach or suggest the compounds of claims 20 and 21, or the complexes of claim 31, and claims 20, 21, and 31 are therefore patentable over John or Largent (whether the references are taken alone or in combination).

One of ordinary skill in the art would not be motivated to make the combination suggested in the Office Action, and would not have a reasonable expectation of success in making the suggested modification. Thus, there would be neither motivation, nor a reasonable expectation of success, in making the combination suggested in the Office Action.

Applicants respectfully contend that it would not have been obvious to combine the teachings of the references as suggested by the Office Action, and that the present claims are not rendered unpatentable by either of the cited references, whether taken alone or in combination. Withdrawal of the rejection is proper and such action is requested.

#### CONCLUSION

Early and favorable consideration of the application is earnestly solicited.

If any extension of time is required, Applicants conditionally petition for any necessary extension. The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 58345(70207), Customer No. 21874.

Application No.: 10/534,225  
Response dated November 18, 2010

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Docket No.: 58345(70207)

Dated: November 18, 2010

Respectfully submitted,

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